**Supplementary Table One** Local guidelines for investigations in children with early developmental impairment and costs over time frame of study

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| **Blood samples**  Full blood count £3.75  Zinc protoporphyrin / haematimics £13.79  Renal function £3.47  Liver function £3.47  Thyroid function £5.94  Bone profile (calcium and phosphate) £3.45  Plasma amino acids £82.00\*  Biotinidase £53.00\*  Creatine kinase (boys only) £3.41  Lead level £15\*  Chromosome (pre 2012 - £120) or microarray (post 2012) £300.00\*  Fragile X if suspected by family history £80.00\*  **Urine samples**  Organic acids £82.00\*  Glycosaminoglycans (if older than three months) £20.00\*  **Total cost of all tests on our guideline:** £669.28  **Other recommendations (not studied in this article)**  Audiology referral  Ophthalmology referral – not mandatory, to consider if concerns  **Magentic resonance imaging under general anaesthetic** (not part of guideline but performed in 55% of cases and found to have high yield) £932.00\* |

\*Costs incurred to a district general hospital for test (as few hospitals seeing children with EDI have metabolic laboratories. All other, unasterisked, costs are local prices)

**Supplementary table 2:** Summary of genetic diagnoses made

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| **Diagnostic microarray results** |
| * Chromosome 1p36,13 deletion (3 cases) * Chromosome 1q21 deletion * Chromosome 1q21 duplication * Chromosome 2p25 deletion * Chromosome 2p16 deletion * Chromosome 2q deletion * Chromosome 4q33 deletion * Chromosome 5q23 deletion (two cases) * Chromosome 5q from q34 to q35 * Chromosome 5 microdeletion * Chromosome 7q11 deletion * Chromosome 7q35 deletion * Chromosome 7p22 duplication * Chromosome 10 duplication with breakpoints within q22.3 and q23.31 * Chromosome 11 deletion with breakpoints q14.1 and q22.1 * Chromosome 11p15 duplication * Chromosome 12 duplication with breakpoints q14.1 and q15 * Chromosome 13q12 deletion * Chromosome 15q11 deletion (four cases) * Chromosome 15q13 deletion (four cases) * Chromosome 15q11 deletion * Chromosome 15 microduplication (three cases) * Chromosome 16p11 duplication (three cases) * Chromosome 16p13 duplication * Chromosome 17q21 deletion * Chromosome 17 duplication with breakpoints q11.1 and q12 * Chromosome 17q12 duplication * Deletion of short arm of chromosome 18 * Chromosome 18q22 deletion * Chromosome 22q11 duplication * Chromosome 22q13 deletion * Chromosome 22q13 deletion * Chromosome Xq26 deletion * Chromosome Xq24 deletion including UBE2a gene * Chromosome 22q11 duplication * Duplication long arm X chromosome including PLP1 gene * Duplication of X chromosome Xq28 (2 cases) |
| **Single gene or clinical diagnoses** |
| Bardet Biedl Syndrome - 5 cases  Neurofibromatosis type 1 - 3 cases  SLC2A1 (GLUT1) mutation - 2 cases  Rett Syndrome - 1 case  Angelman syndrome - 1 case  Kabuki syndrome - 2 cases (1 genetic, 1 clinical)  Cornelia de Lange syndrome - 1 case  Kleefstra syndrome - 1 case  Creatine transport deficiency - 1 case  RYR1 mutation – 1 case  ASPM microcephaly mutation - 1 case  UBE2A mutation - 1 case  PHGDH mutation - 1 case  CASK1 mutation - 1 case  COL4A1 mutation - 1 case  SLC9A6 mutation - 1 case  NRXN1 mutation - 1 case  PLP1 (Pelizaeus-Merzbacher disease) - 1 case  DGUOK (mitochondrial depletion) mutation - 1 case  SLC7A7 mutation (lysinuric protein intolerance) - 1 case  PDHA1 mutation (pyruvate dehydrogenase deficiency) - 1 case  SLC6A8 mutation (creatine transport deficiency) - 1 case  ETHE1 mutation (ethylmalonic aciduria) - 1 case  Tetrasomy 18p - 1 case  Sotos syndrome (clinical diagnosis) - 1 case  Odho symdrome (clinical diagnosis) - 1 case  Atypical ataxia telangiectasia (clinical diagnosis, gene negative) - 1 case  Fetal alcohol syndrome - 1 case |

**Supplementary figure one:** a) The frequency with which additional features were seen in participants; b) the proportion of children with a diagnosis according to additional features; c) the proportion of children with a diagnostic microarray according to additional features; d) the proportion of children with a diagnostic MRI according to additional features